

tibial bowing, severe talipes, hypoplastic scapulae, mental retardation, sex chromosome reversal in some affected females, and severe respiratory difficulties in infancy. One other differential diagnosis of kyphomelic dysplasia is the femoral hypoplasia-unusual facies syndrome which is sporadic<sup>6,7</sup> or rarely autosomal dominant<sup>8</sup> and hence the diagnosis has important counselling differences. Cleft lip and palate has previously only been described in FH-UFS. It now seems that it cannot be used to differentiate the two syndromes,<sup>5</sup> the major difference remaining symmetrical femoral bowing in kyphomelic dysplasia and femoral hypoplasia in the FH-UFS, which is often asymmetrical.

The prognosis appears to be encouraging, but as yet no adults have been described. Femoral angulation improves with age although adult stature is likely to remain short with some limitation of movement at the hips and knees. Cervical subluxation is the most serious complication reported<sup>3</sup> and it must be actively sought. Osteoarthritic problems could be predicted in the future for our patient in view of the osteochondritic changes in the femoral epiphysis.

Apnoea has not previously been reported as a feature of the condition although frequent respiratory infections secondary to a small chest have been described and could be postulated as an underlying cause in our patient.

This case helps to delineate further the features and natural history in this rare skeletal dysplasia.

The authors would like to thank the family of the proband for their cooperation in preparing this report.

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## A case of two inversion (10) recombinants in a family

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**SUMMARY** A family is described in which the mother's four pregnancies resulted in one spontaneous abortion, one healthy boy, and a male and female sib with developmental delay and multiple minor dysmorphic features. Chromosome analysis showed a large pericentric inversion of chromosome 10, involving the region between bands p15.1 and q25.2, in the father and the healthy son: 46,XY,inv(10)(p15.1q25.2), and an unbalanced karyotype in the two affected sibs: rec(10),dup p,inv(10)(p15.1q25.2).

The unbalanced chromosome has been produced by meiotic recombination between the

inversion chromosome and its normal homologue. The two affected sibs have partial duplication of 10p and partial deficiency of 10q, and share a large number of clinical features, several of which have previously been described in both of these chromosome imbalances.

We believe this to be the largest pericentric inversion of chromosome 10 reported to have produced recombinant offspring.

#### Case reports

##### CASE 1

The male proband was the third child of healthy, unrelated parents, born at term by normal vaginal delivery after an uneventful pregnancy. His birth

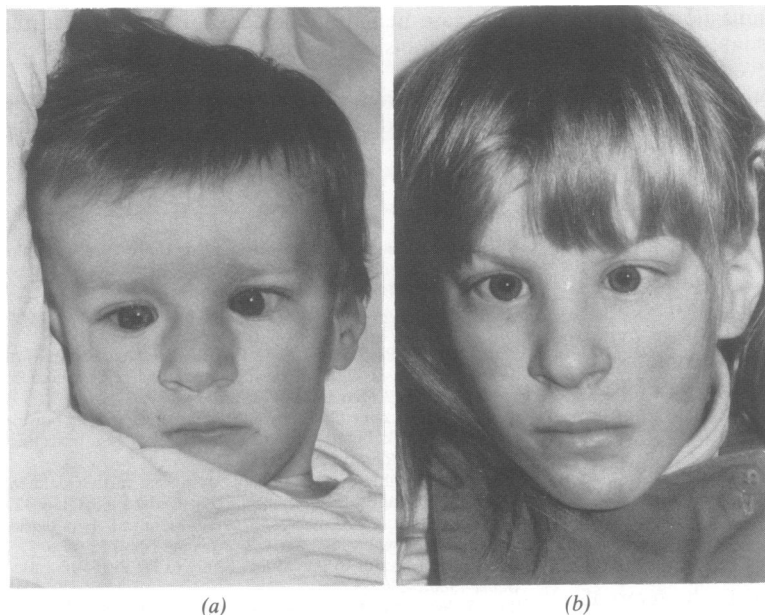


FIG 1 (a) Case 1 at 18 months.  
(b) Case 2 at nine years.

weight was 3500 g (50th centile). He was noted to be floppy, had a weak cry, and had difficulty in establishing feeding. He subsequently showed mild to moderate developmental delay.

Examination at 14 months showed his height and weight to be on the 50th centile, while his head circumference was below the 3rd centile. He had minor dysmorphic features consisting of low set ears, a convergent squint, and a long, prominent nose (fig 1a). He was also noted to have an umbilical hernia, bilateral cutaneous syndactyly of his second and third toes, and bilateral undescended testes.

#### CASE 2

His sister, the oldest of the sibship, was born by normal vaginal delivery at term after an uneventful pregnancy. Her birth weight was 3400 g (50th centile). She required resuscitation in the immediate neonatal period and subsequently also had feeding and respiratory difficulties in the first week. Transient thrombocytopenia of undetermined origin was also observed.

At the age of six months she developed fits, the EEG showing a left sided paroxysmal discharge. Phenytoin controlled her fits at the age of six without further recurrence. She has since exhibited moderate to severe developmental delay with significant behavioural problems and hyperactivity.

Physical examination at the age of eight months showed her weight and head circumference to be on

the 3rd centile, while her height was below the 3rd centile. Her facies was similar to her sib's (fig 1b). Like her sib, she had an umbilical hernia and a mild degree of cutaneous syndactyly of her second and third toes bilaterally.

#### CYTOGENETIC STUDIES

Seventy-two hour lymphocyte cultures released from a methotrexate block with thymidine enriched medium<sup>1</sup> were set up for the three liveborn children and the parents, and used to make GTL banded chromosome preparations. The products of conception from the spontaneous abortion were not available for cytogenetic analysis.

A pericentric inversion of chromosome 10 was found in the father and the healthy son,  $\text{inv}(10)(\text{p}15.1\text{q}25.2)$ , and a recombinant of this inversion was found in the proband and his sister,  $\text{rec}(10), \text{dup } \text{p}, \text{inv}(10)(\text{p}15.1\text{q}25.2)$  (fig 2).

The mother's chromosome analysis was normal. The pedigree is shown in fig 3.

#### Discussion

Duplication/deficiency as a result of meiotic behaviour of pericentric inversions of chromosome 10 has been reported on several previous occasions.<sup>2-5</sup> Two recombinant sibs have been produced in this family and we believe that the large size of the inversion has resulted in an increased possibility for

meiotic recombination. The viability of the two recombinants is explained by the fact that the amount of duplication/deficiency is relatively small. We believe this to be the largest pericentric inversion of chromosome 10 reported to have produced recombinant offspring.

Our two sibs with the recombinant chromosome 10 have partial duplication of 10p and partial deficiency of 10q. It is difficult to discriminate clinically between the phenotypic features contri-

buted by the two chromosomal imbalances. The main diagnostic features of partial duplication 10p were described by Lurie *et al*<sup>6</sup> as dolichocephaly, prominent forehead, wide open sutures and fontanelles, cleft lip and palate, broad root of the nose, club foot, and cystic changes of the kidney. Other features commonly associated include physical and mental retardation, dysplastic ears, heart defects, hypertelorism, and microgenia. Our two affected sibs display only a few of these (table), which

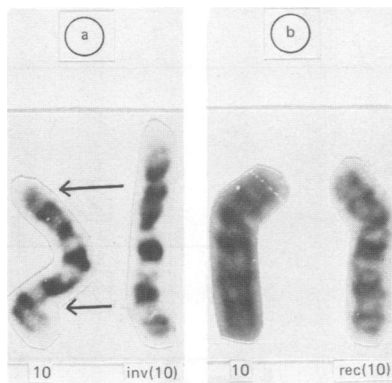


FIG 2 Partial GTL banded karyotypes and schematic representation of the inversion and recombinant 10. (a) Father (inversion 10 on right). (b) Proband (recombinant 10 on right). (c) Normal 10. (d) Inversion event. (e) Inversion 10. (f) recombinant 10.

TABLE The main clinical features of cases 1 and 2 and their correspondence with the features documented by Lurie *et al*<sup>6</sup> for partial duplication 10p and by Shapiro *et al*<sup>7</sup> and Mehta *et al*<sup>8</sup> for partial deficiency 10q.

Clinical findings	Case 1	Case 2	Duplication 10p	Deficiency 10q
Neonatal feeding problems	+	+	-	-
Neonatal respiratory problems	-	+	-	+
Weak cry	+	-	-	-
Hypotonia	+	-	-	+
Low set ears	+	+	+	+
Strabismus	+	+	-	+
Long, prominent nose	+	+	+	+
Physical/mental retardation	+	+	+	+
Developmental delay	+	+	-	+
Behavioural problems	-	+	-	+
Fits	-	+	-	-
Hyperactivity	-	+	-	+
Undescended testes	+	-	+	+
Cutaneous syndactyly	+	+	-	+
Umbilical hernia	+	+	-	-
Thrombocytopenia	-	+	-	-

concurs with the observation by Yunis and Torres de Caballero<sup>2</sup> that partial duplication 10p is not a clinically recognisable entity.

Shapiro *et al*<sup>7</sup> described the main features associated with partial deficiency 10q as respiratory problems at birth, abnormal ears, prominent nasal bridge, hypertelorism, strabismus, and a short or webbed neck. Other common features include low birth weight, microcephaly, developmental delay, and growth retardation. Our two sibs exhibit several of these features (table). The behavioural problems in one child would support the suggestion by Mehta *et al*<sup>8</sup> that behaviour disorder may be a primary feature associated with partial deficiency 10q.

While our two affected sibs show, as one might expect, some of the features described in previously reported cases of partial deficiency 10q, and a few features in common with previously reported cases of partial duplication 10p, the umbilical hernia present in both sibs has not previously been documented in either chromosome imbalance.

The case reports illustrate the potentially high risk for a carrier of a large pericentric inversion of producing viable recombinant offspring and, in this sibship, the considerable degree of overlap of the clinical features seen in such recombinants.

We would like to thank Dr R F Mueller for his advice and involvement.

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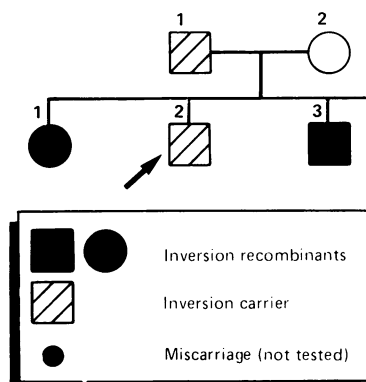


FIG 3 Family pedigree.

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